Data Evaluation Report on the acute dietary toxicity of pyroxsulam to avian species mallard duck (*Anas platyrhynchos*)

PMRA Submission Number 2006-4727 EPA MRID Number 469084-18 APVMA ATS40362

Data Requirement: : PMRA DATA CODE: 9.6.2.5
EPA DP Barcode: D332116
OECD Data Point: IIA 8.1.2
EPA Guideline: 71-2b (850.2200)

Test material: XDE-742 **Purity(%):** 98%
Common name: Pyroxsulam
Chemical name:
IUPAC: N-(5,7-dimethoxy[1,2,4]triazolo[1,5-α]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonamide
CAS name: N-(5,7-dimethoxy[1,2,4]triazolo[1,5-α]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide
CAS No.: 422556-08-9
Synonyms: XDE-742/BAS 770 H/X666742

Primary Reviewer: David McAdam **Date:** 04/12/2006
Australian Government Department of the Environment, Water, Heritage and the Arts (DEWHA)
D. Murphy for D McAdam 22/02/08

Secondary Reviewer(s): Jack Holland **Date:** 21/12/2006
(DEWHA)
22/2/08

Thomas Steeger, Ph.D., Senior Biologist 4/13/08 **Date:** 08/01/2007
U.S. Environmental Protection Agency, EFED, ERB 4

Martin LeMay, M.Sc., Evaluation Officer **Date:** 15/03/2007
Environmental Assessment Division, PMRA Emilie Lavoie for Martin LeMay
05/03/08

Company Code: DWE
Active Code: JUA
Use Site Category: 13, 14
EPA PC Code: 108702

CITATION: Stafford, J. M. 2004. XDE-742– Dietary toxicity test with the mallard duck *(Anas platyrhynchos)*. Springborn Smithers Laboratories, Wareham. Dow AgroSciences, unpublished report, Study No. 040131. 28th December 2004.

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EXECUTIVE SUMMARY:

The subacute dietary toxicity of pyroxsulam to 10-d old mallard ducks *(Anas platyrhynchos)* was assessed over 8 days in accordance with the OPPTS 850.2200 and OECD 205 guidelines. Pyroxsulam was administered to 12 birds in the diet at 0 (control) and 5000 mg/kg diet (nominal); mean measured concentration was 4840 mg ac/kg diet. The 8-day acute dietary LC_{50} was >5000 mg/kg diet (nominal) or >4840 mg ac/kg diet (mean measured). The 8-day NOAEC of pyroxsulam based on mortality was 5000 mg/kg diet (nominal) or 4840 mg/kg diet (mean measured). According to the US EPA classification, pyroxsulam would be classified as practically non-toxic to mallard ducks on a subacute dietary exposure basis using the nominal concentration.

There was no compound related toxicity effects (survival or sublethal) during this 8 day study.

This toxicity study is classified as acceptable for measuring subacute dietary toxicity of pyroxsulam in mallard ducks.

Results Synopsis

Test Organism Size/Age:	10 days old, mean weight of 131.9 g
LC_{50}:	>5000 mg/kg diet (nominal); >4840 mg ac/kg diet (mean, measured). 95% C.I.: Not reported.
NOAEC:	5000 mg/kg diet; 4840 mg ac/kg diet. Probit Slope: Not reported
Endpoint(s) Effected:	There was no compound-related effects (survival or sublethal) noted during this study. The nominal dietary exposure of 5000 mg ac/kg diet was equivalent to a daily dose of 1254 mg/kg body weight/day.
Probit Slope:	Not applicable

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: Springborn protocol "Mallard duck *(Anas platrhynchos)* dietary toxicity test (LC50) with XR-742. Following OPPTS 850.2200 and OECD 205."

OECD protocol Testing of Chemicals 205 "Avian Dietary Toxicity Test" (OECD, 1984).

US EPA. 1996. Avian Dietary Toxicity Test, OPPTS 850.2200. Ecological Effects Test Guidelines.

COMPLIANCE: This study was conducted in accordance with the OECD principles of GLP. Signed and dated GLP and Quality Assurance statements were provided.

A. MATERIALS:

1. Test Material Pyroxsulam (XDE-742)

Description: Solid, white beige

Lot No./Batch No. : E0952-52-01 (ID: TSN 103826)

Purity: 98% active constituent

Stability of Compound Under Test Conditions: The analytical analyses showed that pyroxsulam was stable in the feed over 14 days.

Storage Conditions of Test Chemicals: Stored at ambient temperature in the dark.

Physicochemical properties of XDE-742 *(from company report)*

Parameter	Values	Comments
Water solubility at 20°C	pH 4 0.0164 g/L pH 6 0.0626 g/L pH 7 3.2 g/L pH 9 13.7 g/L	Turner (2004a) Turner (2004a) Turner (2004a) Turner (2004a)
Vapor pressure	$<1 \times 10^{-7}$ Pa at 20 °C	Madsen (2003)
UV absorption	NA	
pKa	4.670	Cathie (2004)
Kow	pH 4 0.097 pH 7 0.024 pH 9 12.1	Turner (2004b) Turner (2004b) Turner (2004b)

2. **Test organism**:

Species: Mallard duck (*Anas platyrhynchos*)
Age at study initiation: 10 days
Weight at study initiation: 131.9 g (114.5-150.2 g)
Source: Whistling Winds, Inc., Hanover, Illinois.

B. STUDY DESIGN:

1. Experimental Conditions

a) Range-finding Study: No range finding study was conducted. Based on the results of the acute oral study, a limit test was selected for the definitive dietary study with two groups; control and 5000 mg/kg feed.

b) Definitive Study

Table 1 Experimental Parameters

Parameter	Details	Remarks
		Criteria
Acclimation		

Parameter	Details	Remarks *Criteria*
Period: Conditions (same as test or not): Feeding: Health (any mortality observed):	9 days before test Same as test Daily basal diet (Purina® Game Bird Startena® (lot #063APR2804) Good health, mortality was zero.	Acclimation acceptable. *OECD requires at least 7 days of acclimation*
Pen size and construction materials	61 X 183 X 61 cm, polycarbonate-coated wire mesh.	Guideline conditions met *EPA requires: about 35 x 100 x 24 cm; OECD requires: 300 cm^2 for bobwhite and 600 cm^2 for mallard*
Test duration	5 days of treated feed and 3 days of clean feed, 8 days test in total.	Guideline conditions met. *EPA/OECD requires: 5 days with treated feed and at least 3 days observation with "clean" feed.*
Test concentrations Nominal: Measured:	0 (control) and 5000 mg/kg feed 0 (control) and 4840 mg/kg feed	Acceptable for a limit test *Four minimum, 5 or 6 strongly recommended, in a geometric scale, unless LC_{50} > 5000 mg ai/kg diet.* Measured conc. should be 80% of the nominal
Solvent/vehicle, if used Type: Amount:	Acetone (70 mL; 1.12% v/wt) Corn oil (98 mL; 1.5% w/w)	Additional 20 mL of acetone was used to rinse out glassware. Guideline met. *EPA requires: Distilled water, corn oil, propylene glycol, 1% carboxymethylcellulose, or gum arabic. Solvent not more than 2%.*
Diet preparation and feeding	*Control diet:* 50 mL acetone; 98 mL corn oil; 20 mL acetone based rinsate; Basal diet (6 kg) *Treated diet:* 50 mL acetone; 98 mL corn oil and 20 mL acetone based rinsate Test substance (30 g); Basal diet (6 kg)	The study states that the acetone evaporated during mixing. Guideline conditions met *EPA requires: Control group tested with diet containing the maximum amount of vehicle used in treated diets*

Parameter	Details	Remarks *Criteria*
Was detailed description and nutrient analysis of the basal diet provided (Yes/No)	Yes	
Indicate whether stability and homogeneity of test material in diet determined (Yes/No)	Yes	
Feed withholding period	Not reported	Not a requirement of the US or OECD Guidelines
Number of birds per replicate/groups For negative control: For vehicle control: For treated:	12 birds in each replicate 24 birds in control 12 in test concentration 5000 mg/kg feed	Guideline conditions met *EPA requires: 10 birds each (strongly recommended)*
Number of replicates/group (if used) For negative control: For vehicle control: For treated:	2 x control 1 x test	
Test conditions Temperature: Relative humidity (%): Photoperiod:	Temp: 22-30°C adjusted according to the age of the birds. Relative humidity 60-74% 14 h light and 10 h darkness	Test conditions within US EPA 850.220 and OECD requirements; Guideline conditions met *Brooder temperature:* *EPA: about 35°C (95°F)* *Room temperature:* *EPA: 22-27°C (71-81°F);* *OECD: range of 22-38 °C based on bird age and species (see OECD 205)* *Relative humidity:* *EPA: 30-80%* *OECD: 50-85% based on bird species (see OECD 205)* *Photoperiod:* *EPA: Minimum of 14 h of light* *OECD: 12-16 h of light*
Reference chemical, if used Name: Concentration tested:	Not applicable	

2. Observations:

Table 2 Observations

Parameters	Details	Remarks
		Criteria
Parameters measured (mortality/body weight/ mean feed consumption/ others)	Mortality, body weight, feed Consumption; morbidity/intoxication	*OECD : the mortality in the controls should not be exceed 10% at the end of the test.*
Indicate the stability and homogeneity of test chemical in the diet	Homogeneity: mean 96.7% Stability: Day 5 = 100% Day 14: 101%	The homogeneity ranged from 116 to 88.3% of nominal excluding one sample at 198 % of nominal, which was treated as an outlier. This is acceptable.
Indicate if the test material was regurgitated	Not reported	Study indicates no abnormal behavioral observations.
Treatments on which necropsies were performed	Postmortem examinations were conducted on 8 surviving birds from the control group and 4 from the treatment group	Guideline conditions met
Observation intervals	3 times on day 1 and twice daily thereafter	Guideline conditions met
Were raw data included?	Yes	

II. RESULTS AND DISCUSSION:

A. **MORTALITY**: No mortality occurred during the study. Therefore, the LC_{50} was empirically determined to be >5000 mg/kg feed (nominal). Based on mean feed consumption, concentration in diet and average body weights for day 0 and day 5, the study report indicates that 5000 mg/kg feed corresponds to 1254 mg/kg bw/day (not required by Guideline).

Table 3 Effect of pyroxsulam (XDE-742) on mortality of Mallard ducks

Treatment Nominal 5000 mg/kg diet mean measured 4840 mg ac/kg diet	**No. of birds per treatment**	**Cumulative mortality**	
		day 5	**day 8**
Solvent/vehicle control	24	0	0
Test concentration	12	0	0
LC_{50}	>5000 mg/kg feed (nominal)		
NOAEC	5000 mg/kg feed (nominal) or 4840 mg/kg feed (mean measured)		
Reference chemical	Not applicable		

B. SUB-LETHAL TOXICITY ENDPOINTS:

No abnormal behavioural observations occurred during the study and no abnormal findings were noted during the post-mortem examinations. Mean changes in body weight were not significantly different among groups at any time during the study. There was no compound related toxicity effects (survival or sub-lethal, including feed consumption) during this 8 day study.

Table 4: Sublethal effect of XDE-742 on Mallard duck.

Treatment Nominal 5000 mg/kg diet mean measured 4840 mg ac/kg diet	Observation							
	Body weight, g			Food consumption, g/day			Other endpoint	
	Day 0	Day 5	Day 8	Day 1	Day 5	Day 8	Day 0	Day 8
Control 1	136.4	287.4	362.0	56.5	60.3	70.0	NA	NA
Control 2	131.0	279.4	347.2	52.9	60.7	64.0	NA	NA
Test concentration 5000 mg ac/kg	128.4	271.3	342.9	51.9	55.9	69.8	NA	NA
EC_{50}	Not applicable (no adverse effects)							
NOAEC	5000 mg/kg feed (nominal) or 4840 mg/kg feed (mean measured)							
Reference chemical	Not applicable							

C. REPORTED STATISTICS: Body weight data taken prior to start of treated feed was analyzed using Levene's Test for homogeneity of variance among cages. Statistical analyses were conducted to determine whether significant differences in change in body weight existed between the control and the treatment group. Body weight data sets were first checked for normality using Chi-square test and for homogeneity of variance using Levene's test. Dunnett's test was used for mean differences between the treatment group and the control group. As these are standard statistical tests, they are acceptable methods.

D. VERIFICATION OF STATISTICAL RESULTS BY THE REVIEWER: Statistics not analyzed. It could be determined visually that there were no adverse effects on body weight or food consumption.

Statistical Method:
LC_{50}: Not applicable
NOAEC: 4840 mg ac/kg feed (mean measured)
Probit Slope: Not applicable

E. STUDY DEFICIENCIES: No significant deficiencies noted. A minor deficiency noted was:

- Study was conducted as a limit test but this is not included in the Guideline (see reviewer's comments).

Several deviations from the protocol were listed in the study report. These were minor changes to the brooder temperatures, the temperature under the brooder heaters and temperature during the test. While these were deviations from the test protocol, they weren't deviation from US EPA or OECD guideline requirements.

These minor deficiencies did not affect the acceptability of the study.

F. REVIEWER'S COMMENTS: The study is a limit test but the test guideline used (US EPA OPPTS 850.2200) does not include reference to a limit test but the OECD TG 205 does. Although not entirely consistent with US EPA Guideline requirements for testing multiple treatment concentrations, this limit test is a scientifically sound method for compounds with no toxicity to the test organisms and is consistent with OECD testing guidelines and as such is considered by the reviewer to be acceptable.

G. CONCLUSIONS: The study is classified as acceptable. The LD_{50} was >4840 mg ac/kg feed and the NOAEC was 4840 mg ac/kg feed (mean measured values). Pyroxsulam is rated as practically non-toxic to mallard ducks in this subacute dietary toxicity study.

III. REFERENCES:

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